UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/314,161	05/19/1999	MICHAL EISENBACH-SCHWARTZ	EIS-SCHWARTZ	4767

1444 7590 12/05/2001

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	15

DATE MAILED: 12/05/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/314,161	Applicant(s) EISENBACH-SCHWARTZ ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *3,9-15,17,18 and 20-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-37* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I-A, claims 1-8, 16, and 19, drawn to a method for preventing or inhibiting neuronal degeneration in the CNS in Paper No. 14 (14 September 2001) is acknowledged. The traversal is on the ground(s) that the treatment of the CNS and the PNS do not require different ingredients, process steps, and end points. Applicant asserts that there is no justification for treating the CNS/PNS dichotomy any differently from the injury/disease (species) dichotomy also discussed. This is found persuasive because of Applicant's persuasive arguments and data in the specification. Therefore, Groups I-A and II-B have been rejoined. Applicant's election with traverse of the "injury" as the species of nervous system defect in Paper No. 14 (14 September 2001) is acknowledged. The traversal is on the grounds that the claims are directed to a method which is identical regardless of whether that which is being treated is an injury or a disease. Applicant contends that it is inappropriate to consider the two patentably distinct. Applicant also asserts that all the method steps are the same and the only difference is in the preamble. This is not found persuasive. An injury and a disease are patentably distinct. An injury is a wound or other specific damage while a disease is an abnormal condition of an organism or part that impairs normal physiological functioning, especially as a result of infection, weakness, or environmental stress. It is noted that the statement at the end of the previous Office Action (Paper No. 13, 14 June 2001) directing the Applicant to select one invention from I-A and II-B and one species from the group of nervous system defects is not a subspecies requirement. It is a reminder for the Applicant to select a species of either i) injury or ii) disease. The spinal cord injury was elected previously as a

species of injury in Paper No. 12 (25 April 2001) in response to the restriction requirement of Paper No. 9 (28 February 2001). It is also noted to Applicant that the species of activated T cells (see claim 4) have been rejoined. This species requirement was made in Paper No. 9 (28 February 2001) and the election by Applicant was made in Paper No. 12 (25 April 2001).

The requirement is still deemed proper and is therefore made FINAL.

It is also noted to Applicant that the species of NS-specific activated T cells recited in claim 4 have been rejoined. The original species requirement was set forth in Paper No. 9 (28 February 2001).

Claims 3, 9-15, 17-18, and 20-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12 and 14 (25 April 2001 and 14 September 2001, respectively).

Claims 1-2, 4-8, 16, and 19, as read upon NS-specific activated T cells and injury, are under consideration in the instant application.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a).

Specification

2. The disclosure is objected to because of the following informalities:

2a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "A METHOD FOR REDUCING SECONDARY NEURONAL DEGENERATION BY ADMINISTERING MBP-SPECIFIC ACTIVATED T CELLS".

Appropriate correction is required.

Claim Objections

3. Claim 1 is objected to because of the following informalities:

3a. The phrase "for ameliorating" in line 3 of claim 1 should be amended to read "to ameliorate".

3b. Claims 1, 2, and 19 recite non-elected species.

Appropriate correction is required.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-2 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3 and 16 of copending Application No. 09/218,277. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims in the '277 application and the instant application recite a method of administering to an individual in need thereof an effective amount of an ingredient selected from the group consisting of NS-specific T cells, a NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen. The recitation of preventing or inhibiting neuronal degeneration to ameliorate the effects of injury or disease in the preamble of the claims from the '277 application and the instant application is interpreted as an intended use and bears no accorded patentable weight. Regarding both applications, the administration of the same recited agents to an individual will elicit the same response in the body, regardless of the phrasing of the preamble. The only difference between the claims of the '277 application and the claims of the instant application is the specific individual administered the agent and the type of NS-specific activated T cells. The claims of the '277 application which recite administering an agent to a human and one agent selected from the group to be administered consists of non-recombinant, NS-specific antiself activated T cells render obvious the pending genus claims of the instant application that recite administering an ingredient to an individual and one agent selected from the group to be administered consists of NS-specific activated T cells. The claims in the instant application encompass the limitations recited in the '277 application. Therefore, the instant claims of a method of administering to an individual in need thereof an effective amount of an ingredient selected from the group

consisting of NS-specific T cells, a NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen is not patentably distinct over the co-pending claims in Application No. 09/218,277.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2, 4-8, 16, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing secondary neuronal degeneration in the central nervous system or peripheral nervous system to ameliorate the degenerative effects of spinal cord injury or blunt trauma comprising administering to an individual in need thereof a composition consisting of activated T cells sensitized to myelin basic protein (MBP) wherein the MBP-activated T cells reduce secondary neuronal degeneration, does not reasonably provide enablement for a method of preventing or inhibiting neuronal degeneration in the central nervous system or peripheral nervous system for ameliorating the effects of injury or disease, comprising administering to an individual in need thereof at least one active ingredient selected from the group consisting of NS-specific activate T cells, a NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method for preventing or inhibiting neuronal degeneration in the central nervous system or peripheral nervous system for ameliorating the effects of injury or disease, comprising administering to an individual in need thereof at least one active ingredient selected from the group consisting of NS-specific activated T cells, NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen. The claims recite that the injury is spinal cord injury and that the T cells are autologous or allogeneic T cells sensitized to human NS antigen. Further, the claims recite that the active ingredient is administered orally and the individual is actively immunized to build up a critical T cell response.

The specification teaches that rats are intraperitoneally injected with activated T cells immediately after optic nerve injury. The degree of primary damage and secondary degeneration of the optic nerve axons and attached retinal ganglion cells is measured by injection of a dye distal to the site of the lesion immediately after the injury. The specification discloses that only the myelin basic protein (MBP) specific T cells limit the extent of secondary degeneration (pg 53-54; Figure 3C). The specification also teaches intraperitoneal injection of adult rats with MBP-specific activated T cells after a calibrated spinal cord contusion is produced (pg 60-62). Locomotor activity, including the trunk, tail, and hindlimbs, of the rats is evaluated twice a day for 3 months (pg 63-64; Figure 7A-7B). Retrograde labeling of the descending spinal tracts is also performed by applying dye below the site of the damage (pg 63-64; Figure 8). The

specification teaches an increase in motor activity in rats after the treatment of MBP-specific activated T cells as compared to controls, suggesting the MBP-specific T cells reduce secondary neuronal degeneration caused by spinal cord injury. The results in the specification also teach that sections of red nuclei from injured rats treated with MBP-specific T cells contain more labeled cells as compared to sections from untreated injured rats, indicating a reduction in injury-induced functional deficit. Diffusion anisotropy in axial sections of the spinal cord show sparing of the spinal tracts and a higher degree of neuron viability in rats treated with MBP-specific T cells (pg 64; Figure 9). However, the specification does not teach preventing or inhibiting neuronal degeneration in any individual by administration of NS-specific activated T cells. The terms "preventing" and "inhibiting" are interpreted as meaning that an activity will not occur, i.e. neuronal degeneration will not occur. Undue experimentation would be required of the skilled artisan to determine the quantity of MBP-specific activated T cells administered, the best route of administration, the duration of treatment, and any possible side-effects to *completely* prevent and inhibit neuronal degeneration in the central nervous system or peripheral nervous system. The specification also does not teach reducing secondary neuronal degeneration by administration of any other NS-specific activated T cells other than MBP-specific activated T cells. Specifically, the results in the specification indicate that OVA-specific and p277-specific T cells do not reduce secondary neuronal degeneration in retinas (pg 54: Figures 2 and 3). Undue experimentation would be required of the skilled artisan to sensitize T cells to every nervous system antigen and administer the cells to an individual to reduce neuronal degeneration. Furthermore, the specification discloses that MBP-specific activated T cells are administered to an individual intraperitoneally rather than orally as recited in claim 16. Relevant literature

reports that limited success has been achieved delivering proteins and peptides orally because of: 1) poor intrinsic permeability across intestinal epithelium, 2) susceptibility to enzymatic attack, 3) rapid post-absorptive clearance, and 4) chemical instability (Pettit et al. Trends Biotech 16: 343-349, 1998; see pg 344-345). Therefore, if proteins and peptides are difficult to deliver orally, one skilled in the art would not expect T cells to be successfully delivered orally, particularly since cells are larger than proteins and peptides. Additionally, the specification does not teach that individuals are actively immunized at any time point prior to the injury to build up a critical T cell response.

Due to the large quantity of experimentation necessary to prevent or inhibit neuronal degeneration by administering any NS-specific activated T cells, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of administering any NS-specific T cells to an individual, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-2, 4-8, 16, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Regarding claims 1-2, 4-8, and 16 , the acronyms "NS and HLA" render the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

9. Claims 1-2, 4-8, 16, and 19 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that the active ingredient prevents or inhibits neuronal degeneration in the central nervous system or peripheral nervous system. Regarding claim 19, there is no step indicating that the activated T cells banked for future use will inhibit or prevent neuronal degeneration.

10. The term "effects" in claims 1-2, 4-8, 16, and 19 is a relative term which renders the claim indefinite. The term "effects" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. There is no stated function or effect to be achieved. The metes and bounds of "effects" to be ameliorated is indefinite because no effects are specified by the claim. (Please note that is issue could be overcome by amending the claims to recite "degenerative effects" rather than "effects".)

11. Claim 16 recites the limitation "said composition" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

12. The term "actively immunized" in claim 16 is a relative term which renders the claim indefinite. The term "actively immunized" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what the individual is immunized with—the NS-specific activated T cells? What is the difference between "active immunization" and "immunization"? How far in advance is the individual "actively immunized" before the injury?

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 4-6, 8, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Popovich et al. (J Neurosci Res 45: 349-363, 1996).

Popovich et al. teach the intravenous administration of myelin basic protein (MBP) activated T cells into naïve recipient rats (pg 353, col 1-2). Popovich et al. also teach that the MBP-activated T cells are T cells from other donor animals (allogeneic). The T cells are cultured with MBP *in vitro* before being injected into the donor animals (pg 353, ¶ 3). Popovich et al. disclose that MBP is an antigenic component of central nervous system myelin and that when placed in complete Freud's adjuvant, produces an acute or remitting-relapsing paralytic disease, i.e., experimental autoimmune encephalomyelitis (EAE). (pg 352, ¶ 3-4; pg 353, ¶ 3).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Gold et al. U.S. patent 6,319, 892

Cohen et al. U.S. patent 5,114,721

Tanabe et al. Science 274: 1115-1123, 1996.

Hauben et al. Lancet 354 : 286-287

Cohen et al. J Neuroimmunol 100 : 111-114, 1999.

Hauben et al. J Neurosci 20(17) : 6421-6430, 2000.

Moalem et al. J Neuroimmunol 106 : 189-197, 2000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

BEB
Art Unit 1647
November 28, 2001